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International variation in rates of uptake of preventive options in *BRCA1* and *BRCA2* mutation carriers

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Abstract

Several options for cancer prevention are available for women with a *BRCA1* or *BRCA2* mutation, including prophylactic surgery, chemoprevention and screening. The authors report on preventive practices in women with mutations from 9 countries and examine differences in uptake according to country. Women with a *BRCA1* or *BRCA2* mutation were contacted after receiving their genetic test result and were questioned regarding their preventive practices. Information was recorded on prophylactic mastectomy, prophylactic oophorectomy, use of tamoxifen and screening (MRI and mammography). Two thousand six hundred seventy-seven women with a *BRCA1* or *BRCA2* mutation from 9 countries were included. The follow-up questionnaire was completed a mean of 3.9 years (range 1.5–10.3 years) after genetic testing. One thousand five hundred thirty-one women (57.2%) had a bilateral prophylactic oophorectomy. Of the 1,383 women without breast cancer, 248 (18.0%)

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had had a prophylactic bilateral mastectomy. Among those who did not have a prophylactic mastectomy, only 76 women (5.5%) took tamoxifen and 40 women (2.9%) took raloxifene for breast cancer prevention. Approximately one-half of the women at risk for breast cancer had taken no preventive option, relying solely on screening. There were large differences in the uptake of the different preventive options by country of residence. Prophylactic oophorectomy is now generally accepted by women and their physicians as a cancer preventive measure. However, only the minority of women with a *BRCA1* or *BRCA2* mutation opt for prophylactic mastectomy or take tamoxifen for the prevention of hereditary breast cancer. Approximately one-half of women at risk for breast cancer rely on screening alone.

Keywords

BRCA1; *BRCA2*; prevention; breast cancer; ovarian cancer

Women with a *BRCA1* or *BRCA2* mutation have a lifetime risk of developing breast cancer of between 45 and 87%.[1,2] Through the identification of women at high-risk, cases of breast and ovarian cancer will be prevented. However, the success of such an approach depends on the acceptance of effective cancer prevention options. There are several options available, varying in levels of effectiveness. Prophylactic mastectomy offers the greatest reduction in breast cancer risk (~95%)[3]. Prophylactic oophorectomy before the age of 40 is associated with a 50% reduction in the risk of breast cancer[4] and an 80% reduction in the risk of ovarian/peritoneal cancer.[5] Tamoxifen has been shown to reduce the risk of breast cancer risk by 50% in women at high-risk of developing breast cancer.[6] In addition, tamoxifen has been shown to prevent contralateral breast cancer in women with a *BRCA1* or *BRCA2* mutation.[7] MRI has been shown to be a more effective screening tool than mammography in studies of *BRCA1* and *BRCA2* mutation carriers in numerous countries.[8–10]

A few studies have examined the rates at which various preventive options are adopted by *BRCA1* and *BRCA2* carriers. These reports suggest that the uptake of preventive procedures differs according to country.[11–16] These differences are likely to be due to many factors, including patient preferences, physician preferences and access to care. In our study, we present data on an international cohort of *BRCA1* and *BRCA2* carriers.

Methods

Study population

Eligible subjects were drawn from a database of carriers of deleterious mutations in either the *BRCA1* or the *BRCA2* gene. These women have been assessed for genetic risk at 41 centers within 9 countries (Austria, Canada, France, Israel, Italy, Norway, Holland, Poland and USA) and were found to carry a *BRCA1* or *BRCA2* mutation. All study subjects provided written informed consent for genetic testing. The study has been approved by the ethics committees of all participating centers. In most cases, testing was offered initially to women who were affected either by breast or ovarian cancer. When a mutation in either the *BRCA1* or *BRCA2* gene was found in a proband or in her relative, testing was offered to other at-risk women in her family. However, in some cases (fewer than 10% of total) an affected woman in the family was not available for study and an unaffected woman was the first member of the family to be tested. Mutation detection was performed using a range of techniques, but in all nucleotide sequences were confirmed with direct sequencing of genomic DNA. A woman was eligible for the study when the molecular analysis established that she was a mutation carrier. We studied both unaffected and affected women with breast cancer.

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Subjects were eligible for this study if they were known to be a *BRCA1* or *BRCA2* mutation carrier, were between 25 and 80 years old, and had no previous history of cancer, other than breast cancer. Subjects who had been diagnosed with unilateral breast cancer before genetic testing were included, but women who were diagnosed with breast cancer during the follow-up period were excluded. All subjects had at least 18 months of follow-up after genetic testing and were alive at the date of follow-up.

Procedures

Subjects completed a baseline questionnaire at the time of genetic testing, which assessed cancer history, and past use of cancer prevention options and screening tests. Follow-up questionnaires were administered by telephone or by mail. Questions assessed the uptake of various cancer preventive options, including prophylactic surgery (mastectomy or oophorectomy), chemoprevention (tamoxifen/raloxifene) and/or breast MRI. The questionnaire is available upon request. In addition, the collaborating investigator from each center was asked whether or not each of the 5 preventive options was discussed and/or recommended to the appropriate patients in their center.

Statistical analysis

The chi-square test was used to compare frequencies of categorical variables, such as different preventive options among regions, and ANOVA was used to compare the mean values of continuous variables among different regions. All statistical tests were done by statistical software SAS version 9.1.3, SAS Institute, Cary, NC, USA.

Results

Four thousand four hundred four women with a *BRCA1* or *BRCA2* mutation were identified; of these, 2,677 were eligible. We excluded 1,727 women: 180 women were less than 25 years, 23 women were greater than 80 years, 438 women had died, 530 women had ovarian cancer, 33 women had been followed for less than 18 months and 164 women were diagnosed with breast cancer during the follow-up period. In addition, 146 women refused to complete the follow-up questionnaire and 213 women were lost to follow-up.

A follow-up questionnaire was completed on the 2,677 eligible women a mean of 3.9 years after genetic testing (range 1.5–10.3 years). Forty-eight women received genetic testing and counseling in Austria (from 1 center), 766 women in Canada (from 14 centers), 31 women in France (from 1 center), 165 women in Israel (from 3 centers), 46 women in Italy (from 1 center), 177 women in Norway (from 1 center), 660 women in Poland (from 1 center), 81 women in Holland (from 1 center) and 703 women in the United States (from 18 centers). One thousand two hundred ninety-four women (48.3%) had a previous diagnosis of unilateral breast cancer. Characteristics of the subjects are presented in Table I. The mean age of the subjects at time of genetic testing was 45.6 years (range 25–79 years) (Table I).

Prophylactic mastectomy

Of the 1,383 women with no history of breast cancer, 248 (18.0%) had a prophylactic bilateral mastectomy (Table II). The mean age at the time of prophylactic mastectomy was 40.7 years. 244 of the 248 prophylactic mastectomies were performed before the age of 60. Women from the United States had the highest rate of prophylactic mastectomy (36.3%). The country with the lowest rate of mastectomy was Poland (2.7%) (Table V).

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Prophylactic oophorectomy

One thousand five hundred thirty-one women (57.2%) had a bilateral prophylactic oophorectomy (Table III). Approximately half of the women had the surgery before genetic testing and half had the surgery after genetic testing. We were unable to distinguish between oophorectomies that were done for cancer prophylaxis or for another reason. A higher proportion of women with a history of breast cancer had a prophylactic oophorectomy (65.7%) than women without breast cancer (42.9%) ($p < 10^{-4}$). In all countries except for Poland, at least 50% of the women had prophylactic oophorectomy. Women from Norway had the highest rate of prophylactic oophorectomy (73%) (Table V).

Tamoxifen/raloxifene

Of the 1,134 women without breast cancer and without a prophylactic mastectomy, only 76 (5.5%) took tamoxifen for chemoprevention of breast cancer. In addition, 40 women (2.9%) reported having taken raloxifene, although this may have been for treatment of osteoporosis, chemoprevention or both (Table IV). Women from the United States were the most likely to take one of the two chemopreventive drugs (12.4%). No women from Norway, Italy, Holland or France reported taking either of the 2 drugs, but these samples were relatively small. There was no significant difference in the uptake of chemoprevention between *BRCA1* carriers (7.4%) and *BRCA2* carriers (9.0%) ($p = 0.43$). In women without breast cancer, tamoxifen use was higher among women who had had an oophorectomy (15.6%), than among women who had not undergone a prophylactic oophorectomy (1.7%).

MRI and mammography

Of the 1,134 women without breast cancer and without prophylactic bilateral mastectomy, data were available for 981 women regarding MRI usage. Three hundred women (30.6%) had been screening for breast cancer using MRI at some point. The majority of these women (91.9%) were screened below the age of 60. There were large differences in the uptake according to country; 94.6% of women from Holland had an MRI, compared to only 2.2% of women from Israel (Table V).

In contrast, 87.5% of women without breast cancer and without a prophylactic mastectomy had at least one mammogram. Mammography uptake was greater than 93% in all countries, except for Poland where mammography uptake was only 65.5%. Most women (83.7%) began mammography screening before genetic testing, however, 16.4% of the women had their first mammogram after receiving the genetic test result.

No preventive option

When all women at risk for first primary breast cancer were considered, 45.8% of the women without breast cancer had chosen no active cancer prevention option (mastectomy, oophorectomy or tamoxifen/raloxifene) (Table VI). Of these, only 19.5% had had an MRI, but 75.0% had had a mammogram.

Discussion

There is a growing evidence that breast and ovarian cancer are preventable in women with a *BRCA1* or *BRCA2* mutation. It is important that the effectiveness of each preventive option be evaluated. However, it is also important that studies be conducted to determine the level of interest of patients and their physicians in endorsing these options, if the potential benefits are to be realized. Hartmann *et al*. suggest that prophylactic mastectomy reduces the risk of breast cancer by 80% in women with a family history of breast cancer,[17] and by 89% risk reduction

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in women with a *BRCA1* or *BRCA2* mutation.[3] Meijers-Heijboer *et al*. also found a significant reduction in the risk of breast cancer associated with prophylactic mastectomy.[18]

The preventive removal of the ovaries and fallopian tubes can provide significant reductions in risk of both breast and ovarian cancers in women with a *BRCA1* or *BRCA2* mutation. The most recent estimate, based on a large prospective study, suggests that the risk reduction for ovarian/fallopian/peritoneal cancer is ~80%.[5] Prophylactic oophorectomy has also been shown to reduce the risk of breast cancer in premenopausal women with a *BRCA1* or *BRCA2* mutation. For women who had preventive surgery before age 40, a 50% risk reduction in breast cancer has been observed.[4] The effectiveness of tamoxifen for primary prevention of breast cancer in *BRCA1* carriers is not yet proven and its use in this setting is not widespread. However, tamoxifen has been shown to reduce the risk of contralateral breast cancer in both *BRCA1* and *BRCA2* carriers by 50%.[7,19]

There are reasons why women may not elect for a cancer prevention option. Many women with a *BRCA1* and *BRCA2* mutation believe that they have inadequate information to make a decision.[12] In addition, women may feel that their psychosocial functioning may be compromised, including their perception of body image after prophylactic mastectomy. Many are worried about sexual functioning after prophylactic mastectomy or oophorectomy.[20] Many women are concerned about the side-effects of tamoxifen.[21] In addition, in some countries, access to care may be a limiting factor.[21,22]

A representative from each study group was questioned regarding the content of the typical counseling session. Physicians and counselors from all centers routinely discuss prophylactic mastectomy and prophylactic oophorectomy as preventive options, and recommend the use of MRI for screening in women with a *BRCA1* or *BRCA2* mutation. Tamoxifen is recommended in some genetics centers in Canada, the USA and Poland, but chemoprevention with tamoxifen is not currently recommended in Italy, Austria, Holland, Israel, France or Norway. With the exception of a single patient from Austria, no western European patient used tamoxifen (21 Polish patients used tamoxifen). In certain countries, cost may also be an issue—for example in the United States, patients may be required to pay (in part or in full) for their MRI.

We observed striking differences in the rates of uptake of all of the cancer preventive options from country to country, however, in some countries the number of cases included were small and some were based on only one clinical center. It is unclear why such marked differences are present. Previous studies have reported on uptake of cancer preventive options by *BRCA1* and *BRCA2* mutation carriers in single countries[12,13,15,16,21–24] In one study, 344 women attended a cancer genetics clinic for the first time were surveyed about their preferences regarding cancer prevention.[25] The authors included women from Canada (Quebec), France and Great Britain. The authors attributed the observed variations to cultural differences between the countries. However, we have recently reported on the uptake rates of preventive procedures by Canadian women with a *BRCA1* or *BRCA2* mutation.[26] All these women received genetic testing and counseling in Canada, nevertheless, the uptake of cancer preventive options varied greatly across the country. Assuming that cultural differences among patients within Canada are minimal, it suggests that cultural differences may not entirely explain the variations in the uptake rates—more likely differences were due to health care providers' recommendations and continuity of follow-up care. As expected, physicians have differing opinions on the effectiveness of various preventive options. In Maryland, USA, surgeons were surveyed about prophylactic mastectomy. A greater proportion of plastic surgeons (85%) than general surgeons (47%) or gynecologists (38%) agreed that bilateral prophylactic mastectomy had a role in the care of high-risk women.[27] In France, only 11% of French physicians found it acceptable to propose prophylactic mastectomy to women with a *BRCA* mutation.[28]

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Peshkin *et al*.[29] surveyed physicians regarding recommendations for tamoxifen for primary breast cancer prevention. The physicians were more likely to recommend tamoxifen to *BRCA2* carriers (73%) than to *BRCA1* carriers (57%) ($p < 0.0001$). The authors concluded that physicians were not convinced of the benefits of tamoxifen in *BRCA1* and *BRCA2* mutation carriers. Although this research did not examine the actual uptake rates of the preventive options by women based on their physicians' recommendation, it is interesting that a much higher proportion of physicians reported that they would recommend tamoxifen than the fraction of women who reported taking it in our study. Furthermore, we observed similar rates of tamoxifen usage among women with *BRCA1* and *BRCA2* mutations. Very few women in Europe had taken tamoxifen. A few had taken raloxifene, but it is likely that this was prescribed for osteoporosis. This is most likely due to current recommendations by these countries. The only European country that does recommend tamoxifen is Poland, where the uptake was 6%. In our study, tamoxifen use was positively correlated with oophorectomy, *i.e*., its use was more common in women with a risk of breast cancer already lowered by oophoretomy.

The countries that contributed to this study have different health care systems and policies, and access to services may explain some of the observed variance. In Canada and most European countries, preventive surgery, including reconstruction, is available to all women at no cost (in the context of a universal health care system). It is interesting that the highest rates of preventive surgery were reported in the United States, a country in which most women rely on private health insurance. This observation may be reflective of the type of women who initially present for genetic testing in the United States. The cost of genetic testing is ~$4,000, and therefore it may only be available to women with private health insurance or individuals who can afford the test.

The use of screening MRI varied widely between countries, and yet all countries included in our study recommend MRI for *BRCA1* and *BRCA2* mutation carriers. Women in Holland, Austria and Italy had the highest uptake rates (above 60% for all). This may be because women from these countries are eligible for research studies investigating the effectiveness of MRI as a screening modality for women with a *BRCA1* or *BRCA2* mutation. A surprising result of this study was the low uptake of MRI by women in the United States (24.4%), given that American women had high rates for the surgical preventive options. Recently, Saslow *et al*. at the American Cancer Society published guidelines for breast screening with MRI.[30] Annual MRI screening was recommended for any women with a *BRCA1* or *BRCA2* mutation. The publication of these guidelines may influence the uptake of MRI in the future.

In most of the countries surveyed, the majority of women had elected for at least one cancer preventive option. However, only 26.3% of women without breast cancer in Poland had taken a preventive option. Only 6.4% of women from Poland had a screening MRI and only 65.5% had mammography. Genetic testing is widely available to Polish women, but the provision of follow-up services to women who test positive may not be keeping pace. Furthermore, in Poland, genetic testing is offered to women with only a modest family history of breast or ovarian cancer and these women may not feel they are at as high of risk as women from families with multiple cases. Previous research suggests that cancer risk perception influences uptake of preventive procedures.[31]

There are several limitations to our study. The patients studied here may not be a representative of all women within a country that have received genetic testing for *BRCA1* or *BRCA2*. Our study subjects were women who attended one of 41 specialized genetic counseling centers from 9 countries. We do not have information about women who attended other genetic testing centers. In some countries the total number of subjects included was small, and the subjects were from a single clinical center and therefore may not be representative. Results from these countries must be interpreted with caution. Furthermore, the patients were tested on average,

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7 years ago, and patterns of practice have evolved since 1999. We believe that genetic services are now better integrated with surgical care and screening programs and that physician attitudes have changed with regards to specific preventive measures. It is our intention to repeat this survey in 5 years time in order to evaluate trends in clinical practice.

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Appendix

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TABLE I

CHARACTERISTICS OF 2,677 MUTATION CARRIERS IN FOLLOW-UP STUDY BY 9 COUNTRIES

Variables	Austria, *N* = 48 (1.8%)	Canada, *N* = 766 (28.6%)	France, *N* = 31 (1.2%)	Israel, *N* = 165 (6.2%)	Italy, *N* = 46 (1.7%)	Holland, *N* = 81 (3.0%)	Norway, *N* = 177 (6.6%)	Poland, *N* = 660 (24.7%)	USA, *N* = 703 (26.3%)	All, *N* = 2,677 (100%)	*p* Value[1]
Mutation number (%)											
BRCA1	38 (79.2)	448 (58.5)	25 (80.7)	95 (57.6)	36 (78.3)	63 (77.8)	176 (99.4)	660 (100)	510 (72.6)	2,051 (76.6)	$<10^{-4}$
BRCA2	10 (20.8)	311 (40.6)	6 (19.4)	56 (33.9)	10 (21.7)	18 (22.2)	1 (0.6)	0	188 (26.7)	600 (22.4)	
BRCA1+2	0	7 (0.9)	0	0	0	0	0	0	5 (0.7)	12 (0.5)	
BRCA1 or 2	0	0	0	14 (8.5)	0	0	0	0	0	14 (0.5)	
Mean year of											
Birth	1957.2	1953.2	1951.5	1953.1	1957.0	1958.2	1955.4	1958.3	1953.4	1954.9	$<10^{-4}$
Range	1931–71	1917–77	1935–68	1920–74	1933–74	1933–76	1921–75	1923–79	1916–77	1916–79	
Mean age at											
Baseline interview	42.9	46.6	47.1	47.2	43.6	42.7	45.0	45.0	46.0	45.6	0.001
Range	28–68	25–79	30–62	25–79	25–66	25–68	26–78	25–79	25–79	25–79	
Subjects with											
Breast cancer number (%)	23 (47.9)	373 (48.7)	27 (87.1)	70 (42.4)	26 (56.5)	26 (32.1)	42 (23.7)	321 (48.6)	386 (54.9)	1,294 (48.3)	$<10^{-4}$
Mean age at diagnosis	39.5	42.5	41.4	43.6	40.0	41.3	42.3	43.8	40.4	42.0	0.003
Range	27–56	24–75	25–60	20–78	29–58	31–53	26–61	24–70	21–73	20–78	
Mean year at											
Baseline interview	2000.1	1999.9	1998.6	2000.3	2000.7	2000.9	2000.4	2003.0	1999.4	2000.6	$<10^{-4}$
Range	1999–02	1994–05	1997–01	1996–02	1997–04	2000–02	1997–02	1999–05	1994–05	1994–05	
Mean years of											
Follow-up	4.1	4.4	5.9	4.1	4.8	4.3	3.6	2.6	4.4	3.9	$<10^{-4}$
Range	1.9–5.9	1.6–10.1	2.9–7.1	1.7–8.6	2.0–9.0	2.0–5.8	2.3–6.5	1.5–7.3	1.6–10.3	1.5–10.3	

[1] ANOVA for differences in mean values between the 9 countries, chi-square test for the differences in frequency distributions of the 9 countries.

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TABLE II

PROPHYLACTIC MASTECTOMY FOR WOMEN WITHOUT BREAST CANCER

Age	Number (%)	No prophylactic mastectomy	Had prophylactic mastectomy[1] (%)	Timing of prophylactic mastectomy	
				Before genetic testing	After genetic testing
No breast cancer					
(25, 35)	379 (27.4%)	323	56 (14.7%)	10	46
(35, 60)	911 (65.9)[1]	723	188 (20.6%)	80	108
(60, 70)	66 (4.8%)	63	3 (4.6%)	1	2
70 and +	26 (1.9%)	25	1 (3.9%)	1	0
Total	1,382 (100.0)	1,134 (82.1)	248 (18.0)	92 (6.7)	156 (11.3)

[1]One subject in this age group was missing data on prophylactic mastectomy.

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TABLE III

PROPHYLACTIC OOPHORECTOMY BY BREAST CANCER STATUS

Age	Number (%)	No prophylactic oophorectomy	Had prophylactic oophorectomy (%)	Timing of prophylactic oophorectomy	
				Before genetic testing	After genetic testing
All women					
(25, 35)	442 (16.5)	378	64 (14.5)	14	50
(35, 40)	444 (16.6)	222	222 (50.0)	84	138
(40, 60)	1,512 (56.5)	433	1,079 (71.4)	537	542
(60, 70)	201 (7.5)	72	129 (64.2)	95	34
70 and +	78 (2.9)	41	37 (47.4)	29	8
Total	2,677 (100.0)	1,146 (42.8)	1,531 (57.2)	759 (28.4)	772 (28.8)
No breast cancer					
(25, 35)	379 (27.4)	329	50 (13.2)	11	39
(35, 40)	275 (19.9)	155	120 (43.6)	44	76
(40, 60)	637 (46.1)	186	451 (70.8)	230	221
(60, 70)	66 (4.8)	17	49 (74.2)	34	15
70 and +	26 (1.9)	15	11 (42.3)	8	3
Total	1,383 (100.0)	702 (50.8)	681 (49.2)	327 (23.6)	354 (25.6)
With breast cancer					
(25, 35)	63 (4.9)	49	14 (22.2)	3	11
(35, 40)	169 (13.1)	67	102 (60.4)	40	62
(40, 60)	875 (67.6)	247	628 (71.8)	307	321
(60, 70)	135 (10.4)	55	80 (59.3)	61	19
70 and +	52 (4.0)	26	26 (50.0)	21	5
Total	1,294 (100.0)	444 (34.3)	850 (65.7)	432 (33.4)	418 (32.3)

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TABLE IV

TAMOXIFEN AND RALOXIFENE IN WOMEN WITHOUT BREAST CANCER AND WITHOUT PROPHYLACTIC MASTECTOMY

Age	Number in age group (%)	No chemoprevention number (%)	Tamoxifen number (%)	Raloxifene number (%)
(25, 35)	379 (27.4%)	376 (99.2)	3 (0.8)	0 (0)
(35, 60)	912 (65.9)	811 (88.9)	68 (7.5)	33 (3.6)
(60, 70)	66 (4.8%)	55 (83.3)	4 (6.1)	7 (10.6)
70 and +	26 (1.9%)	25 (96.2)	1 (3.9)	0 (0)
Total	1,383 (100.0)	1,267 (91.6%)	76 (5.5)	40 (2.9)

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TABLE V

UPTAKE OF OPTIONS BY COUNTRY

Variables	Austria, N^1 = 48, N^2=25, N^3 = 20	Canada, N^1 = 766, N^2 = 393, N^3 = 305	France, N^1 = 31, N^2 = 4, N^3 = 3	Israel, N^1 = 165, N^2 = 95, N^3 = 91	Italy, N^1 = 46, N^2 = 20, N^3 = 18	Holland, N^1 = 81, N^2 = 55, N^3 = 37	Norway, N^1 = 177, N^2 = 135, N^3 = 128	Poland, N^1 = 660, N^2 = 339, N^3 = 330	USA, N^1= 703, N^2 = 317, N^3 = 202	*p* Value[4]
Prophylactic oophorectomy[1] (*n* = 2,667)	25 (52.1%)	439 (57.3%)	22 (71.0%)	110 (66.7%)	23 (50.0%)	52 (64.2%)	130 (73.5%)	230 (34.9%)	500 (71.1%)	$<10^{-4}$
Prophylactic mastectomy[2] (*n* = 1,382)	5 (20.0%)	88 (22.4%)	1 (25.0%)	4 (4.2%)	2 (10.0%)	18 (32.7%)	6 (4.5%)	9 (2.7%)	115 (36.3%)	$<10^{-4}$
Mammography[3] (*n* = 1,133)	20 (100%)	294 (96.7%)	3 (100%)	87 (95.5%)	18 (100%)	37 (100%)	119 (93.0%)	216 (65.5%)	197 (97.5%)	$<10^{-4}$
MRI[5] (*n* = 1,134)	13 (65.0%)	146 (47.8%)	2 (66.7%)	2 (2.2%)	13 (72.2%)	35 (94.6%)	18 (14.1%)	22 (6.7%)	49 (24.4%)	$<10^{-4}$
Tamoxifen/ raloxifene[5] (*n* = 1,134)	1 (5.0%)	30 (9.8%)	0 (0%)	10 (11.0%)	0 (0%)	0 (0%)	0 (0%)	21 (6.4%)	25 (12.4%)	0.001

[1] All subjects.

[2] Subjects without breast cancer; one subject with missing data on mastectomy excluded.

[3] Subjects without breast cancer and without prophylactic mastectomy; one subject with missing data on mammography excluded.

[4] chi-square test for the differences in frequency distributions of the 9 countries.

[5] Subjects without breast cancer and without prophylactic mastectomy.

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TABLE VI

UPTAKE OF AT LEAST ONE CANCER PREVENTION OPTION (PROPHYLACTIC MASTECTOMY, PROPHYLACTIC OOPHORECTOMY OR TAMOXIFEN) IN WOMEN WITHOUT BREAST CANCER

	Austria (*N* = 25)	**Canada (*N* = 393)**	**France (*N* = 4)**	**Israel (*N* = 95)**	**Italy (*N* = 20)**	**Holland (*N* = 55)**	**Norway (*N* = 135)**	**Poland (*N* = 339)**	**USA (*N* = 317)**
At least one cancer prevention option	10 (40.0%)	232 (59.0%)	3 (75.0%)	55 (57.9%)	8 (40.0%)	31 (56.4%)	92 (68.2%)	89 (26.3%)	229 (72.2%)

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